

## **PATHOPHYSIOLOGIC CHANGES IN A MURINE MODEL OF BETA-THALASSEMIA: HUMAN HEMOGLOBIN E TRANSGENE INTEGRATION**

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Hemoglobin E (HbE; Codon 26, G>A) is the most common hemoglobin variant found in Southeast Asians. We generated a novel C57BL/6 transgenic murine model of the HbE thalassemia. In HbE-transgenic mice, one or both alleles of mouse  $\beta$ -globin genes were removed by breeding with  $\beta$ -knockout mice to produce double heterozygous and  $\beta$ -thalassemia/HbE rescued mice, respectively. As reported earlier, rescued mice developed anemia similar to  $\beta$ -thalassemia in people. Here we further define clinicopathologic changes in these mice. Double heterozygous mice had minimal changes in erythrocyte (RBC) shape (poikilocytosis), few target cells and no significant difference in red cell indices when compared with wild type mice. However, poikilocytosis was present in the  $\beta$ -thalassemia/HbE rescued mice and its severity depended on the number of copies of the  $\beta^E$ -globin gene integrated into mouse chromosome. The mean half-time (T1/2) RBC survival in double heterozygotes was  $39.63 \pm 1.53$  days with a RBC life span of  $54.21 \pm 3.26$  days. The mean T1/2 RBC and life span in the rescued mice were  $12.76 \pm 2.25$  and  $37.50 \pm 3.39$  days, respectively. At necrosy splenomegaly and hepatomegaly were present in rescued mice but not in double heterozygous mice. Histologic examination of spleen and liver revealed iron accumulation in both mouse types and variable degrees of increased extramedullary hematopoiesis in the spleen and liver of rescued mice. These results indicated that the  $\beta$ -thalassemia/HbE mice that have  $\beta^E$ -transgene under homozygous  $\beta$ -knockout background develop pathophysiologic changes similar to  $\beta$ -thalassemia in people. Study of this murine model will further elucidate the pathogenesis of  $\beta$ -thalassemia and enable us to test new therapeutic regimes, such as  $\beta$ -globin-stimulating agents, iron chelators and gene therapy. This study was supported in part by Thai Government Annual Research Budget 2004 to P.W. and Thailand Research Fund to S.F. as a Senior Research Scholar.

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## **THE EPIDEMIOLOGIC HISTORY OF JAPANESE ENCEPHALITIS (JE) IN SOUTHERN THAILAND AND THE IMPACT OF ROUTINE JE VACCINATION IN THE REGION**

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**Background:** Chiang Mai experienced the first (1969) major JE outbreak in Thailand. During the 1980's, northern and central provinces consistently reported JE disease. In 1989, the Thai